WEST Search History

DATE: Wednesday, June 26, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L5	L4 and liposome$	23	L5
L4	(carbonate) adj5 (glycerol)	541	L4
L3	(carbonate) adj10 (glycerol)	773	L3
L2	(carbonate) adj10 (distearoyl adj1 glycerol)	0	L2
L1	(carbonate) adj5 (distearoyl adj1 glycerol)	0	L1

END OF SEARCH HISTORY

L5: Entry 8 of 23 File: USPT Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051576 A
TITLE: Means to achieve sustained release of synergistic drugs by conjugation

Detailed Description Paragraph Right (26):
The codrug of the invention may be administered in injectable form selected from the group consisting of liposomes, liquids, suspensions and microsphere nanoparticles. Preparation of such aqueous solutions, liposomes, emulsion and suspensions are known to those of ordinary skill in the art (see Remington's Pharmaceutical Sciences, 18th Ed., Mack Publishing Co., Easton, Pa., 1990, pp. 1504-1712, incorporated herein by reference).

Detailed Description Paragraph Right (75):
The following is the structure of 5FU linked via a carbonate bond to a glycerol diflurbiprofen ester. The rationale is that the compound would hydrolyze in vivo to release 5FU, glycerol and two molecules of flurbiprofen.

CLAIMS:

4. A codrug according to claim 3, wherein said injectable form is selected from the group consisting of liposomes, suspensions, microsphere and nanoparticles.

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L3: Entry 11 of 58 File: USPT May 2, 2000

DOCUMENT-IDENTIFIER: US 6056973 A
TITLE: Therapeutic liposome composition and method of preparation

Drawing Description Paragraph Right (4):
FIG. 4 is a plot showing the blood circulation lifetime of target-cell sensitized liposome prepared in accordance with the invention, where the percent of injected dose in vivo for liposomes having E-selectin Fab fragments targeting ligands (30 ligands per liposome represented by solid triangles, 70 ligands per liposome represented by solid squares) and for liposomes having a surface coating of polyethyleneglycol chains (open circles) as a function of time after dosing; and

Drawing Description Paragraph Right (5):
FIGS. 5A-5B are scanned images of micrographs of blood vessels in a window chamber of a mouse dorsal fold, where FIG. 5A is the control of the untreated blood vessels under transmitted light, and FIG. 5B is a fluorescence micrograph showing binding of fluorsecin-labeled liposomes bearing an E-selectin Fab fragments to endothelial cells in the blood vessels.

Detailed Description Paragraph Right (66):
In studies performed in support of the invention, a targeting conjugate of the ligand sialyl-Lewis.sup.x was attached to PEG-DSPE according to known methods (DeFrees, S. A., et al., J. Am. Chem. Soc., 118:6101-6104 (1996)). Sialyl-Lewis.sup.x can be used to target liposomes to cells expressing endothelial leukocyte adhesion molecule-1 (ELAM-1 or E-selectin) for delivery of a therapeutic agent to a site of inflammation. ELAM-1 is expressed on the surface of endothelial cells of blood vessels adjacent to sites of inflammation. ELAM-1 recognizes and binds the polysaccharide moiety sialyl-Lewis.sup.x which is present on surfaces of neutrophils, and recruits neutrophils to sites of inflammation.

Detailed Description Paragraph Right (75):
Liposomes having an E-selectin Fab fragment targeting ligand were prepared in accordance with the invention for in vivo administration to rodents. As described in Example 2, an anti-E-selectin Fab fragment was conjugated to PEG-DSPE to form an E-selectin Fab-PEG-DSPE targeting conjugate. The targeting conjugate was incubated with pre-formed .sup.111 In-labelled-liposomes composed of partially hydrogenated soy phosphatidylcholine (PHPC), PEG-DSPE and cholesterol in a 55:40:3 molar ratio in an amount sufficient to obtain 12, 20, 33, 40 and 70 Fab residues per 100 nm liposome (Example 2B). The insertion procedure resulted in greater than 95% of the targeting conjugates being inserted into the pre-formed liposomes. In one embodiment of the invention, the insertion efficiency is greater than 90%, more preferably greater than 95%.

Detailed Description Paragraph Right (77):
As described in Example 2C, pre-formed liposomes composed of hydrogenated soy phosphatidylcholine (HSPC), cholesterol, PEG-DSPE and fluorescein-labelled DHPE, in a molar ratio of 53.5/40/4/2.5, were incubated with the E-selectin-PEG-DSPE targeting conjugate at 37.degree. C. for 1 hour. The fluorescein-labeled liposomes were administered to mice equipped with a dorsal skin fold window chamber. Endotoxin was applied topically in the window chamber 10 minutes after intravenous injection of the liposomes. FIGS. 5A-5B are scanned images of photomicrographs of the blood vessels under transmitted light prior to liposome administration (FIG. 5A) and 5 hours after administration of the target-cell sensitized, fluorescein-labeled liposomes (FIG.

5B).

Detailed Description Paragraph Right (78):
As can be seen in FIG. 5B, the E-selectin Fab liposomes target the endothelial cells along the blood vessels. The appearance of E-selectin antigen peak was around 5 hours after endotoxin treatment, indicating that the binding activity of the E-selectin antibody was retained.

Detailed Description Paragraph Right (119):
E-selectin Fab-PEG-DSPE targeting conjugate was inserted into pre-formed liposomes as follows. The pre-formed liposomes were composed of hydrogenated soy phosphatidylcholine (HSPC), cholesterol and PEG-DSPE in a molar ratio of 53.5/40/4. The liposomes included 2.5 mole percent of the lipid marker of fluorescein-DHPE (Molecular Probes, Inc.). The pre-formed liposomes were incubated with the micellular solution of the targeting conjugate at 37.degree. C. for 1 hour. The insertion mixture was placed on a Bio-Rad A50m column equilibrated with 25 mM HEPES/saline pH 7.2 and 0.5 ml fractions were collected. Spectrophotometric analysis of the fractions indicated that the insertion efficiency of the Fab targeting conjugate into the liposomes was approximately 100% after 2 hours at 37.degree. C.

Detailed Description Paragraph Center (6):
Preparation of Anti-E-selectin Fab Conjugate and Insertion into Pre-formed Liposomes